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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/010,476	12/07/2001	Norbert O. Reich	G&C 30794.30-US-D1	8266

7590 08/26/2003

Attn: Karen S. Canady
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EXAMINER

MCINTOSH III, TRAVISS C

ART UNIT

PAPER NUMBER

1623

DATE MAILED: 08/26/2003

10

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/010,476

Applicant(s)

REICH ET AL.

Examiner

Traviss C McIntosh

Art Unit

1623

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 12 May 2003.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 21-35 is/are pending in the application.
- 4a) Of the above claim(s) 28-30 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 21-27 and 31-35 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 07 December 2001 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____.
- 4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____.

Detailed Action

The Examiner of the U.S. Patent application SN 10/010,476 has changed. In order to expedite the correlation of papers with the application please direct all future correspondence to the Technology Center 1600, Art Unit 1623, Examiner Traviss McIntosh.

Election/Restrictions

Applicant's election with traverse of Group I in Paper No. 8 is acknowledged. The traversal is on the ground(s) that a search into the prior art with regards to the invention of the different groups is so related that separate and significant search efforts should not be necessary. Applicants assert that at the very least, separate search efforts should not be necessary for groups I and II, as the method of claim 21 is the basis for the method of group II. The examiner agrees with applicants in regards to rejoining groups I and II, however these groups are seen to be independent and distinct from group III. The function of groups I and II is inhibiting methylation, where the function of group III relates to modulating methylation, either increasing or decreasing DCMTase activity thereby inhibiting or enhancing methylation. A reference rendering one of groups I or II obvious would not necessarily render group III obvious. That is, a reference which taught identification of a compound which increases DCMTase activity would not necessarily teach administering a compound which inhibits DCMTase activity inhibits the proliferation of cancer.

The requirement is still deemed proper and is therefore made FINAL.

An action on the merits of claims 21-27 and 31-35 is contained herein below.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 21-27 and 31-35 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Independent claims 21 and 22 both contain the phrase “in the presence of” or “the presence of”. This is not seen as a way to clearly articulate that which applicant intends as their invention, as “in the presence” has not been defined by the claim, and one of ordinary skill in the art would not be apprised of exactly that which applicant intends. “In the presence of” could be in the same room, in the same reaction container, on the same lab table. Clarity is respectfully requested.

All claims which depend from an indefinite claim are also indefinite. *Ex parte Cordova, 10 U.S.P.Q. 2d 1949, 1952 (P.T.O. Bd. App. 1989).*

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

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The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

- Determining the scope and contents of the prior art.
- Ascertaining the differences between the prior art and the claims at issue.
- Resolving the level of ordinary skill in the pertinent art.
- Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 22, 23, 25-27 are rejected under 35 U.S.C. 103(a) as being unpatentable over Szyf et al. (US Patent 5,578,716) in view of Bettelheim et al. (Introduction to Organic and Biochemistry, 4th edition, 1990, Harcourt, Inc.).

Claim 22 is drawn to a method of inhibiting the proliferation of cancer cells in a subject comprising, administering a synthetic inhibitor molecule which binds to an allosteric site on DCMTase, which then inhibits DCMTase-mediated methylation of DNA, which inhibits the proliferation of the cancer cells. Claim 23 limits the cancer cell as being from lung, breast, prostate, pancreas, or colon. Claims 25-27 limit the subject to humans and various animals. Claim 31 limits the inhibitor molecule to comprise a C-5 methylcytosine. Claim 32 limits the inhibitor molecule to an oligonucleotide which comprises a C-5 methylcytosine.

Szyf et al. teach to administer a compound which inhibits DNA methyl transferase have activity as inhibiting tumorigenesis (column 2, lines 48-53). Additionally, Szyf et al. teach the compositions to be effective against human small lung cell carcinoma (sentence bridging column 2 and column 3). What is not taught is to administer a compound which will bind to an allosteric site, thus changing the shape of the active site which in turn inhibits proliferation of cancer cells.

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Bettelheim et al. is cited to teach the definition of allosterism. Allosterism is the process by which an enzyme is regulated by the binding of a regulator (the synthetic inhibitor molecule of the instant application) on one site of the enzyme which modifies the enzymes ability to bind the target substrate at the active site by changing the shape of the active site (see figure 13.12 and discussion). Thus, Bettelheim et al. teach that a regulator binding to the allosteric site will change the shape of the active site, thus inhibiting the enzymes function.

It would have been obvious to one of ordinary skill in the art at the time of the invention to administer the broad genus of a compound which binds to the allosteric site of DCMTase to inhibit cancer proliferation because it is known that inhibiting methyltransferase activity inhibits cancer proliferation and compounds binding to an allosteric site are known to inhibit the enzymes activity. One would be motivated to use an allosteric inhibitor as allosteric inhibitors are known to change the active sites ability to effectively bind to it's target, thus altering the process which the enzyme is regulating.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Traviss McIntosh whose telephone number is 703-308-9479. The examiner can normally be reached on M-F 8:30-5:00.

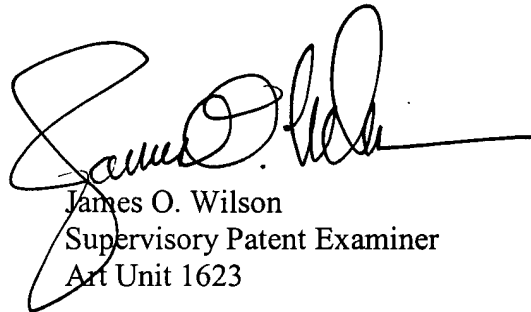
If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James O. Wilson can be reached on 703-308-4624. The fax phone numbers for the

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organization where this application or proceeding is assigned are 703-305-3014 for regular communications and 703-305-3014 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Traviss C. McIntosh
August 22, 2003



James O. Wilson
Supervisory Patent Examiner
Art Unit 1623